

Claims

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1. Osteogenic protein expressed from recombinant DNA in a host cell and capable of inducing endochondral bone formation in a mammal when disposed within a matrix implanted in said mammal;

the protein comprising a pair of oxidized subunits constituting a dimeric species, one of said subunits comprising:

OPS

2. Osteogenic protein expressed from recombinant DNA in a host cell and capable of inducing endochondral bone formation in a mammal when disposed within a matrix implanted in said mammal,

the protein comprising a pair of oxidized subunits constituting a dimeric species, one of said subunits comprising:

OP7

3. Osteogenic protein expressed from recombinant DNA in a host cell and capable of inducing endochondral bone formation in a mammal when disposed within a matrix implanted in said mammal.

the protein comprising a pair of oxidized subunits constituting a dimeric species, one of said subunits comprising:

OPM

wherein the starred residues are optional.

Sub A2

4. Osteogenic protein expressed from recombinant DNA in a host cell and capable of inducing endochondral bone formation in a mammal when disposed within a matrix implanted in said mammal,

the protein comprising a pair of oxidized subunits constituting a dimeric species, one of said subunits comprising:

OPP

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as
Cont*

E	V	H	F	R	S	I	R	S	T	G	S	K	Q	R	S	Q	N	R	S
*	*	*	*	*	*							*	*	*	*	*	*	*	*
K	T	P	K	N	Q	E	A	L	R	M	A	N	V	A	E	N	S	S	S
*	*	*	*																
D	Q	R	Q	A	C	K	K	H	E	L	Y	V	S	F	R	D	L	G	W
Q	D	W	I	I	A	P	E	G	Y	A	A	Y	Y	C	E	G	E	C	A
F	P	L	N	S	Y	M	N	A	T	N	H	A	I	V	Q	T	L	V	H
F	I	N	P	E	T	V	P	K	P	C	C	A	P	T	Q	L	N	A	I
S	V	L	Y	F	D	D	S	S	N	V	I	L	K	K	Y	R	N	M	V
V	R	A	C	G	C	H													

wherein the underlined residues indicate a potential cleavage site for an N-terminal secretion signal peptide and the starred residues indicate a potential cleavage site for protein maturation.

a 5. The invention of claim 1, 2, 3, or 4 wherein said osteogenic protein has an apparent molecular weight of about 27 kD when oxidized as determined by comparison to molecular weight standards in SDS-polyacrylamide gel electrophoresis.

a 6. The invention of claim 5 wherein one subunit of said protein has an apparent molecular weight of about 14 kD and the other has an apparent molecular weight of about 16 kD, both as determined after reduction by comparison to molecular weight standards in SDS-polyacrylamide gel electrophoresis.

a 7. The invention of claim 1, 2, 3, or 4 wherein said osteogenic protein is glycosylated.

a 8. The invention of claim 7 wherein said osteogenic protein has an apparent molecular weight of about 30 kD when oxidized as determined by comparison to molecular weight standards in SDS-polyacrylamide gel electrophoresis.

9. The invention of claim 8 wherein one subunit of said protein has an apparent molecular weight of about 16 kD and the other has an apparent molecular weight of about 18 kD, both as determined after reduction by comparison to molecular weight standards in SDS-polyacrylamide gel electrophoresis.

10. The invention of claim 1, 2, 3 or 4 wherein the other subunit comprises the amino acid sequence:

11. The invention of claim 1, 2, 3 or 4 wherein the other subunit comprises the amino acid sequence:

12. The invention of claim 1, 2, 3, or 4, wherein the other subunit comprises the amino acid sequence:

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OPM

wherein the standard residues are optional.

13. The invention of claim 1, 2, 3, or 4 wherein the other subunit comprises the amino acid sequence:

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wherein the underlined residues indicate a potential cleavage site for an N-terminal secretion signal peptide and the starred residues indicate a potential cleavage site for protein maturation.

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14. The invention of claim 1, 2, 3 or 4 wherein the other subunit comprises the amino acid sequence:

CBMP2AS

V	D	F	S	D	V	G	30	W	N	D	W	I	V	A	P	P	G	40	L	Y
F	Y	C	H	G	E	C	50	P	F	P	L	A	D	H	L	N	S	60	H	A
A	I	V	Q	T	L	V	70	N	S	V	N	S	K	I	P	K	A	80	N	H
P	T	E	L	S	A	I	90	S	M	L	Y	L	D	E	N	E	K	100	C	C
K	N	Y	Q	D	M	V	110	V	E	G	C	G	C	R		V	V	L		

μ

15. The invention of claim 1, 2, 3 or 4 wherein the other subunit comprises the amino acid sequence:

CBMP2AL

V	D	F	S	D	V	G	W	N	D	W	I	V	A	P	P	G	Y	H	A	
F	Y	C	H	G	E	C	P	F	P	L	A	D	H	L	N	S	T	N	H	
A	I	V	Q	T	L	V	N	S	V	N	S	K	I	P	K	A	C	C	V	
P	T	E	L	S	A	P	S	M	L	Y	L	D	E	N	E	K	V	V	L	
K	N	Y	O	D	M	V	V	E	G	C	G	C	R							

16. The invention of claim 1, 2, 3 or 4 wherein the other subunit comprises the amino acid sequence:

CBMP2AM

														K	R				
Q	A	K	H	K	Q	R	K	R	L	K	S	S	C	K	R	H	P	L	Y
V	D	F	S	D	V	G	W	N	D	W	I	V	A	P	P	G	Y	H	A
F	Y	C	H	G	E	C	P	F	P	L	A	D	H	L	N	S	T	N	H
A	I	V	Q	T	L	V	N	S	V	N	S	K	I	P	K	A	C	C	V
P	T	E	L	S	A	I	S	M	L	Y	L	D	E	N	E	K	V	V	L
K	N	Y	Q	D	M	V	V	E	G	C	G	C	R						

17. The invention of claim 1, 2, 3 or 4 wherein the other subunit comprises the amino acid sequence:

CBMP2BS

L	Y	V	D	F	S	D	V	G	W	N	D	W	I	V	A	P	40		
P	G	Y	Q	A	F	X	C	H	G	D	C	P	F	P	L	A	D	H	L
N	S	T	N	H	A	I	V	Q	T	L	V	N	S	V	N	S	S	I	P
K	A	C	C	V	P	T	E	L	S	A	I	S	M	L	Y	L	D	E	Y
D	K	V	V	L	K	N	Y	Q	E	M	V	V	E	G	C	G	C	R	

18. The invention of claim 1, 2, 3 or 4 wherein the other subunit comprises the amino acid sequence:

CBMP2BL

R H S L Y V D F S D V G W N D W I V A P
P G Y Q A F Y C H G D C P F P L A D H L
N S T N H A I V Q T L V N S V N S S I P
K A C C V P T E L S A I S M L Y L D E Y
D K V V L K N Y Q E M V V E G C G C R

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19. The invention of claim 1, 2, 3 or 4 wherein the other subunit comprises the amino acid sequence:

CBMP2BM

A K R S P K H H S Q R A R K K N K N C R
R H S L Y V D F S D V G W N D W I V A P
P G Y Q A F Y C H G D C P F P L A D H L
N S T N H A I V Q T L V N S V N S S I P
K A C C V P T E L S A I S M L Y L D E Y
D K V V L K N Y Q E M V V E G C G C R

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20. A DNA sequence encoding an amino acid sequence sufficiently duplicative of that of the sequence encoded by the gene of Figure 1B such that said encoded sequence induces bone or cartilage formation in dimeric form when implanted in a mammal in association with a matrix.

21. The protein expressed from the DNA of claim 20.

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22. A cell line engineered to express at least one of the subunits of the protein of claim 1, 2, 3, or 4.

23. A cell line engineered to express the DNA of claim 20.

24. An antibody specific for an epitope of the protein of claim 10, 11, or 12.

25. An antibody specific for an epitope of the protein of claim 13.

26. An antibody specific for an epitope of the protein of claim 14, 15, or 16.

27. An antibody specific for an epitope of the protein of claim 17, 18, or 19.